REMARKS

Applicant respectfully requests reconsideration of the present application in view of the foregoing amendments and in view of the reasons that follow.

I. STATUS OF THE CLAIMS

New claims 22-26 have been added.

Claims 2-4 have been cancelled without prejudice or disclaimer.

Claims 1-26 are pending. Claims 14-21 have been withdrawn as non-elected. Thus, claims 1-13 and 22-26 are under examination.

This amendment adds, changes and/or deletes claims in this application. A detailed listing of all claims that are, or were, in the application, irrespective of whether the claim(s) remain under examination in the application, is presented, with an appropriate defined status identifier. The disclosure of Applicant's application provides support for the amendments to the claims. For example, at least page 6, lines 30-35; page 7, lines 24-37; and page 11, line 29, to page 12, line 15, of Applicant's specification provide support for the amendments to the claims.

II. PRIORITY

The Office has not acknowledged Applicant's claim for foreign priority under 35 U.S.C. § 119 and receipt of certified copies of Applicant's priority documents in this National Stage application.

Applicant respectfully requests that the Office acknowledge Applicant's claim and receipt of these documents in the next Office Correspondence, such as by checking all of the relevant boxes in the section "Priority under 35 U.S.C. § 119" of the summary of the correspondence.

III. OBJECTION TO CLAIMS 4-5

Claims 4 and 5 are objected to for allegedly having improper dependent form. Applicant respectfully submits that the amendments to the claims render this objection moot. Reconsideration and withdrawal of this objection is respectfully requested.

IV. REJECTIONS UNDER §§ 101, 112

Claim 12 is rejected under 35 U.S.C. § 101 for allegedly being drawn to non-statutory subject matter and rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite. Applicant respectfully submits that the amendments to the claims render these rejections moot. Reconsideration and withdrawal of these rejections is respectfully requested.

V. INDEFINITENESS REJECTIONS

Claims 1-13 are rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite. Applicant respectfully submits that the amendments to the claims render these rejections moot. Reconsideration and withdrawal of these rejections is respectfully requested.

VI. ART REJECTIONS

The claims as amended are novel and nonobvious over the cited references for the reasons presented below.

A. Novelty

Claims 1-6, 12, and 13 are rejected under 35 U.S.C. § 102(a), 102(e) as allegedly being anticipated by U.S. Pub. No. 2003/0082232 to Lee *et al.* (hereafter "Lee"). This rejection is respectfully traversed.

Lee discloses an adjuvant made of a calcium containing material, such as calcium phosphate and calcium sulfate. See Lee at paragraphs 0023-0025. Lee states that in most cases the adjuvants are resorbable and that magnetic materials can be combined with the adjuvants. See Lee at paragraphs 0027 and 0071.

The Office states on page 10 of the Office Action that Lee does not disclose a particle size of 0.001 to 0.1 microns or 0.1 to 10 microns.

Therefore, Lee does not disclose a biocompatible degradable composite material comprising a degradable biocompatible calcium sulfate matrix, said matrix containing magnetic particles, wherein the magnetic particles have a particle size between 0.001 μm to 10 μm, said material being found as a slurry during its introduction into an organism, as a solid subsequently, and said matrix being resorbed within a period of eight weeks, as recited in claim 1. Claims 5, 6, 12, and 13 depend from claim 1.

Reconsideration and withdrawal of this rejection is respectfully requested.

Claims 1-4, 6-9, and 12 are rejected under 35 U.S.C. § 102(a), 102(e) as allegedly being anticipated by EP 0 361 797 to Kokubo *et al.* (hereafter "Kokubo"). This rejection is respectfully traversed.

Kokubo discloses a ceramic body for use in hyperthermia treatment that includes a body made of 20-90 wt% of ferromagnetic ferrite particles, 80-10 wt% of an inorganic material as a matrix in which the ferrite particles are dispersed. See Kokubo at page 3, lines 41-47. The inorganic material can be at least one of wollastonite, dicalciumsicilicate, hydroxyapatite, a glass consisting of CaO and SiO_2, and a crystallized glass consisting of CaO and SiO_2. See Kokubo at page 3, lines 41-47.

Kokubo does not disclose the biocompatible degradable composite material of claim 1 because Kokubo does not disclose a particle size between 0.001 μm to 10 μm, as recited in claim 1. Kokubo is silent in regard to this feature.

In addition, the matrix of the material of Kokubo is not capable of being resorbed within a period of eight weeks, as recited in claim 1. Kokubo states on page 3, lines 20-24, that although the use of heat is effective to treat cancer cells, the use of metallic substances to generate heat from a magnetic field is not desirable due to noxious metallic ions released by these substances and their low heat-generating efficiencies. Kokubo states on page 3, lines

27-30, that its invention regards a ceramic body that is to be embedded in living tissue and be "innocuous and stable for a long period when embedded in living tissues."

In fact, Applicant has demonstrated that a material of the matrix described in Kokubo would be very stable and only exhibit a resorption zone of a few micrometers after 18 months. Enclosed with this reply is a copy of "Integration of dense HA rods into cortical bone" by Benhayoune *et al.* As discussed in the abstract, hydroxyapatite (HA) samples were implanted into subjects for 2 weeks to 18 months and when the samples were studied the samples exhibited a resorption zone of only a few micrometers after 18 months. This demonstrates that the material used for the matrix of Kokubo is relatively stable and would not be a matrix which is resorbed within a period of eight weeks, as recited in claim 1.

For at least these reasons, Kokubo does not anticipate claims 1, 6-9, and 12. Reconsideration and withdrawal of this rejection is respectfully requested.

B. Nonobviousness

Claims 1-13 are rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Lee in view of "Selective Targeting of Magnetic Albumin Microspheres to the Yoshida Sarcoma: Ultrastructural Evaluation of Microsphere Disposition" by Widder *et al.* (hereafter "Widder"). This rejection is respectfully traversed.

The Office argues on pages 10-11 of the Office Action that Lee incorporates by reference Widder, which discloses the use of magnetic albumin microspheres with an average diameter of 1 micrometer to treat tumors. The Office argues on page 10-11 of the Office Action that it would have been obvious to incorporate the particles of Widder in the material disclosed by Lee because this is one embodiment taught by Lee.

Lee discusses and incorporates by reference Widder in paragraph 0071. Lee states in paragraph 0071 "it may be desirable to combine magnetic materials with the inventive calcium phosphate adjuvants to guide the controlled delivery of the active agent to the target site" (emphasis added). Lee does not disclose or suggest that the particles of Widder can be used with a degradable biocompatible calcium sulfate matrix, as recited in claim 1. Lee does not provide any guidance for combining the magnetic materials of Widder with calcium

sulfate. Instead, Lee only discusses the combination of the magnetic materials of Widder with calcium phosphate materials in paragraph 0071 of Lee. Thus, Lee does not disclose or suggest an embodiment in which magnetic particles are combined with a degradable biocompatible calcium sulfate matrix, as recited in claim 1.

In addition, it would not have been obvious to one skilled in the art to modify the combination of Lee and Widder to provide the magnetic particles of Widder in a calcium sulfate matrix. As discussed above, Lee only discusses the use of magnetic particles in calcium phosphate materials and provides no guidance to use magnetic particles in calcium sulfate. The material of Lee is not designed to be rapidly resorbed to liberate magnetic particle close to tumor cells such that the magnetic particles can be internalized by tumor cells without damaging them. Further, Lee states in paragraph 0071 that magnetic particles may be combined with calcium phosphate adjuvants to guide their controlled delivery to a target site, not to lyse tumor cells by thermolysis.

In contrast, the magnetic particles of Widder are provided without a matrix which can be rapidly resorbed to liberate magnetic particles close to tumor cells such that the magnetic particles can be internalized by tumor cells without damaging them, let alone a matrix of calcium sulfate. Widder is instead concerned with the selective targeting of magnetic albumin microspheres to the Yoshida Sarcoma.

Applicant's biocompatible degradable composite material can provide the following advantages: total or substantially total integration into bone tissue without significant reaction as a foreign body, not interfering or substantially interfering with bone regeneration, targeting magnetic particles close to tumor cells, having a matrix which is resorbed within a period of eight weeks, providing a material which releases magnetic particles in a manner that the particles can be internalized by tumor cells and heated at a reasonable temperature in an electromagnetic field without damaging or substantially damaging the particles, and having good heat generating efficiency while being suited to be embedded in living tissue.

In view of the deficiencies of Lee and Widder, one skilled in the art would not have had any guidance or reason to modify Lee and Widder to provide a biocompatible degradable

composite material comprising, among other things, a degradable biocompatible calcium sulfate matrix containing magnetic particles, as recited in claim 1.

For at least these reasons, the combination of Lee and Widder does not provide the features of claim 1 and it would not have been obvious to combine Lee and Widder to provide the features of claim 1.

Claim 10

Claim 10 depends from claim 1 and is allowable over Lee and Widder for at least the reasons discussed above. Claim 10 further recites "wherein said particles have a particle size between 0.001 and 0.1 μm."

The Office argues on page 11 of the Office Action that although Widder only discloses microspheres having an average diameter of 1 micrometer, "due to particle size distribution inherent in microparticle formulations, it is reasonable that at least some portion of the microparticles have diameters between 0.001 and 0.1 microns."

This is not a proper basis for the obviousness of a claimed range. Widder discloses a diameter which falls outside the claimed range of claim 10. Therefore, Widder does not disclose or suggest a range which overlaps the range recited in claim 10. See MPEP § 2144.05, Part I. Widder only states that the microspheres have an average diameter of 1 micrometer but does not disclose or suggest other sizes or ranges. Widder provides no factual basis for a size range which overlaps the range recited in claim 10.

Instead, the Office argues that such an overlap would be "inherent" because "it is reasonable" that such an overlap would exist. Although inherency is not appropriate in the context of obviousness, such inherency can only be relied upon by establishing a basis in fact and/or technical reasoning to reasonably support a determination that an allegedly inherent characteristic necessarily flows from the disclosure of the prior art. See MPEP § 2112, Part IV, *citing Ex parte Levy*, 17 USPQ2d 1461, 1464 (Bd. Pat. App. & Inter. 1990). Any inherent disclosure may not be established by probabilities or possibilities. See MPEP § 2112, Part IV, *citing In re Robertson*, 49 USPQ2d 1949, 1950-51 (Fed. Cir. 1999). Here, the Office only

relies upon the probability or possibility that a distribution of the microspheres of Widder would have a size falling within the rage recited in claim 10, arguing that such a possibility or probability is "reasonable." However, this is not a proper basis for inherency or the obviousness of a claimed range.

For at least the reasons discussed above, reconsideration and withdrawal of this rejection is respectfully requested.

VII. NEW CLAIMS

New claims 22-26 have been added. Claims 22-26 depend from claim 1 and are allowable over the prior art for at least the reasons discussed above and for their respective additional recitations.

In particular, claim 23 further recites "wherein the magnetic particles have a particle size between 0.05 μm to 0.1 μm." As discussed above, Lee, Kokubo, and Widder do not disclose or suggest such a range of particle size.

CONCLUSION

Applicant submits that the present application is now in condition for allowance. Favorable reconsideration of the application as amended is respectfully requested.

The Examiner is invited to contact the undersigned by telephone if it is felt that a telephone interview would advance the prosecution of the present application.

The Commissioner is hereby authorized to charge any additional fees which may be required regarding this application under 37 C.F.R. §§ 1.16-1.17, or credit any overpayment, to Deposit Account No. 19-0741. Should no proper payment be enclosed herewith, as by the credit card payment instructions in EFS-Web being incorrect or absent, resulting in a rejected or incorrect credit card transaction, the Commissioner is authorized to charge the unpaid amount to Deposit Account No. 19-0741.

If any extensions of time are needed for timely acceptance of papers submitted herewith, Applicant hereby petitions for such extension under 37 C.F.R. §1.136 and authorizes payment of any such extensions fees to Deposit Account No. 19-0741.

Respectfully submitted,

Date 14-Jan-2010

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Biomaterials

Integration of dense HA rods into cortical bone

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Abstract

HA ceramics are daily used in human surgery for bone healing partly due to their ability to integrate into bone. They are generally used under a macroporous form. The behaviour of dense HA after implantation is not so well known. We implanted within cortical sheep femurs dense pure HA-ceramics cylinders for periods from 2 weeks to 18 months. The samples were then sectioned and examined using back-scattered and secondary SEM and the interface was analysed using EDS. Histomorphometry measurement was also performed using an image analysis device coupled to a light microscope. It appeared that the cylinders were in direct contact with immature bone after three weeks. The bone maturated within three months. The implant surface showed moderate signs of resorption and some grains were released from the surface. The resorption zone was only a few μm thick after 18 months. The bulk ceramic contained default zones of increased porosity. They can constitute fragile zone when located close to the surface in which the resorption rate is increased. We conclude that dense pure HA is poorly degraded when implanted in cortical bone. Degradation depends on the defaults found on the ceramic structure and the remodelling of bone surrounding the material.

Keywords: Biomaterials; Hydroxyapatite; Dense; Bone; Interface; Degradation

1. Introduction

Hydroxyapatite (HA) is generally used as a macroporous ceramic with the intention that it is invaded by the healing bone tissue. Macroporous ceramics made of HA and TCP in various proportions are integrated into the bone tissue and are subjected to a creeping substitution process [1]. This leads to the degradation of the ceramic by osteoclasts and macrophages and its replacement by newly formed bone [2,3].

HA is a calcium phosphate phase considered very close to that of bone tissue composed of an A or AB carbonate apatite that is poorly crystallized. HA shows a low solubility at a neutral pH when compared to other calcium phosphate phases having a higher Ca/P ratio. However, when the pH decreases, as in an osteoclast resorption chamber or within macrophage lysosomes, solubility of all CaP ceramics increases dramatically.

The sintering of an HA-slurry leads to the formation of HA-ceramics with various characteristics of porosity, grain size and surface area. Each of these has an influence on the HA-ceramic degradation and integration. Material characteristics are not the only factors acting on the ceramic integration rate. The bone remodelling rate is also involved, which means that the integration process is different in cancellous bone from cortical bone.

Dense HA shows mechanical and surface-related characteristics very different from those of porous ceramics [4]. Their behaviour and the tissue reaction at their surface is unclear. Therefore a dense HA-ceramic implanted in cortical bone for 1 yr has been evaluated with respect to the degradation rate of this material within this environment [5].

2. Materials and methods

2.1. Implant characteristics

The implants were cast in cylinder form 5 mm in diameter and 10 mm in length. They were made of 99.7%

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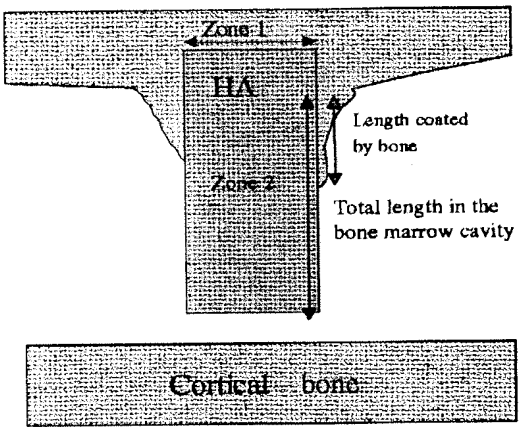

Fig. 1. Section of HA in the cortical bone.

hydroxyapatite: $Ca_{10}(PO_4)_6(OH)_2$. The porosity was less than 5%, the pores were not connected and pore size was under 5 μm. The surface roughness was: Ra = 2 μm, Rp = 4 μm, Rt = 6 μm and the crystallinity 100%.

2.2. Implantation protocol

Three holes were drilled each at a distance of 1.5 cm from the other on the same longitudinal line on the external cortex of mid-diaphysis of sheep's femur. The implants were placed in the external holes and a screw was placed in the central hole in order to make a mark for sectioning.

At different times after implantation (2 weeks, 2, 3, 9 and 18 months) an animal was sacrificed, the femoral mid-diaphysis was harvested and fixed in a 4% formaldehyde solution. The samples were dehydrated in ethanol and defated in a mixture of ethanol–xylene. Then, the bone was embedded in polymethylmethacrylate [6].

Saw cuts of about 300 μm were made perpendicular to the long axis of the cylinders, through the screw, which was apparent at the cortex surface. They were then placed on the surface of a cold setting polystyrene resin and were ground using silicon carbide discs (Fig. 1). Remaining resin material was removed by careful irrigation. For each implantation period one animal and two cylinders were used.

3. SEM method

3.1. Micrographs

The secondary electron micrographs were obtained using a field effect electron microscope LEO, the beam current 5 keV energy being close to 5 μA. The back-scattered electron micrographs were obtained using a JEOL-JSM 5400LV microscope with 15 keV energy and a beam current of some nA (Figs. 2–4).

3.2. EDX measurements

The X-rays intensity profiles shown in Figs. 5–7 were obtained using a scanning electron microscope PHILIPS 501 equipped with a Si(Li) detector. The beam current of 15 keV electron beam was about 9 nA. The beam diameter was close to 1 μm and the scanned line was about 50 μm. The scan line begins in cortical bone at 20 μm from implant edge, then crosses bone-HA interface and finishes in HA at 20 μm from implant edge [7]. The Ca K_α and P K_α X-rays intensities profiles were made at each delay. And each measurement was repeated three times and only the mean value have been conserved in order to avoid all statistic variations.

3.3. Histomorphometry

All measurements, excepted the index of osteoconductivity, were taken from the interface between the ceramic bottom and bone (zone 1, Fig. 1). They were performed under a light microscope coupled to an image analysis device at a 20× magnification.

Five different measurements were made at each period of implantation:

- the ratio of the ceramic length at bone contact to total ceramic length (osseointegration index),
- the porosity of bone in a 0.5 mm thick zone around the implant,
- the thickness of the immature bone in contact with the ceramic,
- the ratio of the ceramic length located in the bone marrow cavity coated by bone to the total length of the ceramic present in the bone marrow (Fig. 1, zone 2). This ratio was designated as osteoconductive index,
- The mean thickness of a 0.1 mm deep zone located beneath the ceramic surface.

4. Results and discussion

Secondary and back-scattered electron micrographs were performed at different times after implantation.

4.1. At 2 weeks

The implant was mostly surrounded by connective tissue interposed between the implant and bone (Fig. 2a). Immature bone formed within this connective tissue. This tissue was different from cortical bone. This grey-level was heterogeneous and the osteocyte density

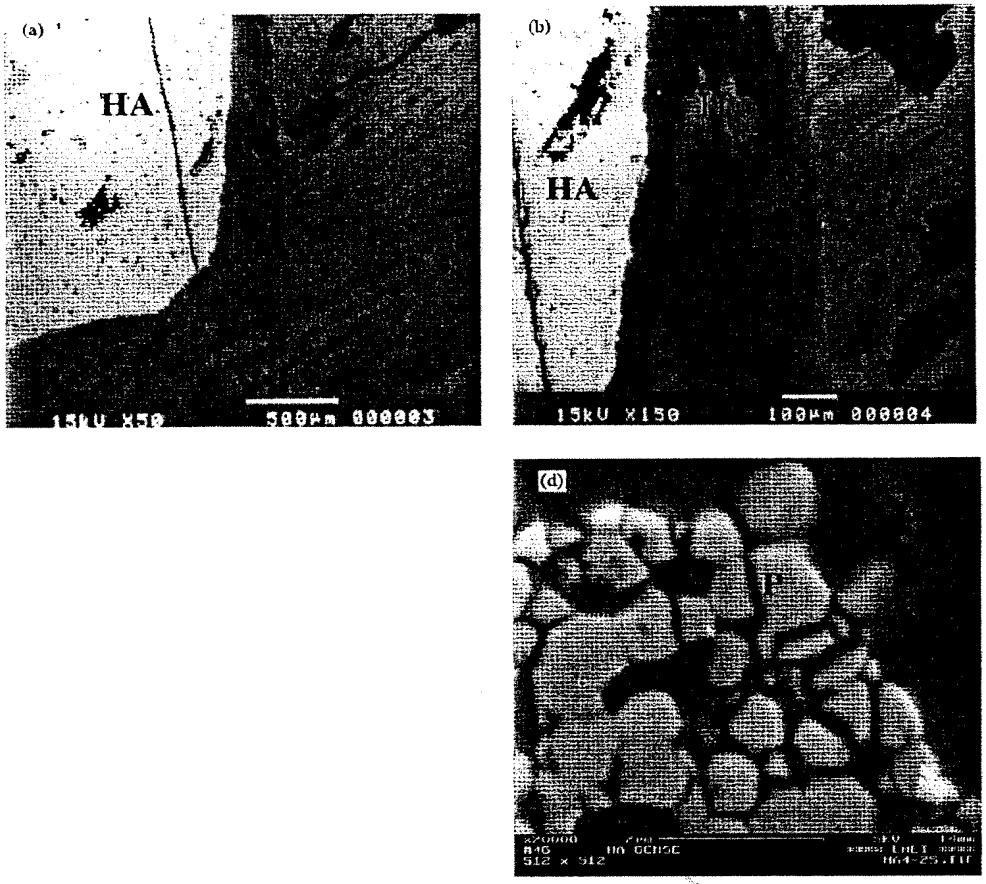

Fig. 2. (a) Back-scattered electron micrograph showing the global view of bone (B)-HA interface 2 weeks after implantation (magnification × 50); (b) back-scattered electron micrograph showing the deposited immature tissue (IT) on the surface of bone cortical edge, 2 weeks after implantation (magnification × 150); (c) secondary electron micrograph showing the remodelling of bone occurring on HA surface 2 weeks after implantation (Ct: connective tissue, magnification × 500); (d) secondary electron micrograph showing the degradation of HA particles (P) interface 2 weeks after implantation (magnification × 20 000).

was higher than in cortical bone. This immature tissue was deposited at the surface of the cortical edge (Fig. 2b).

In some locations, bone was found in contact with the ceramic surface (Fig. 2c). The surface was smooth and small limited surface irregularities were already in evidence. The resorption of HA particles was very active with numerous sub-micron HA particles (P) at the surface of the bioceramic (Fig. 2d). Resorption lacunae were visible in cortical bone close to the implantation site edges. Defaults in the bulk ceramic associated with a higher porosity zone were apparent.

4.2. At 2 months

Immature bone tissue bridged the cortical bone edges to the implant surface (Fig. 3a). The bone in contact with the implant surface did not show a lamellar organization. A marked remodelling process was found in the cortical bone which showed numerous and large resorption lacunae in the periphery of the cavity edges (Fig. 3b). Many defaults were visible in the bulk ceramic. These defaults were constituted by zones with increased porosity. These porous zones were more numerous at the implant surface. Many particles were released from these zones (Fig. 3c).

4.3. At 3 months

No difference was seen between two and three months implanted samples.

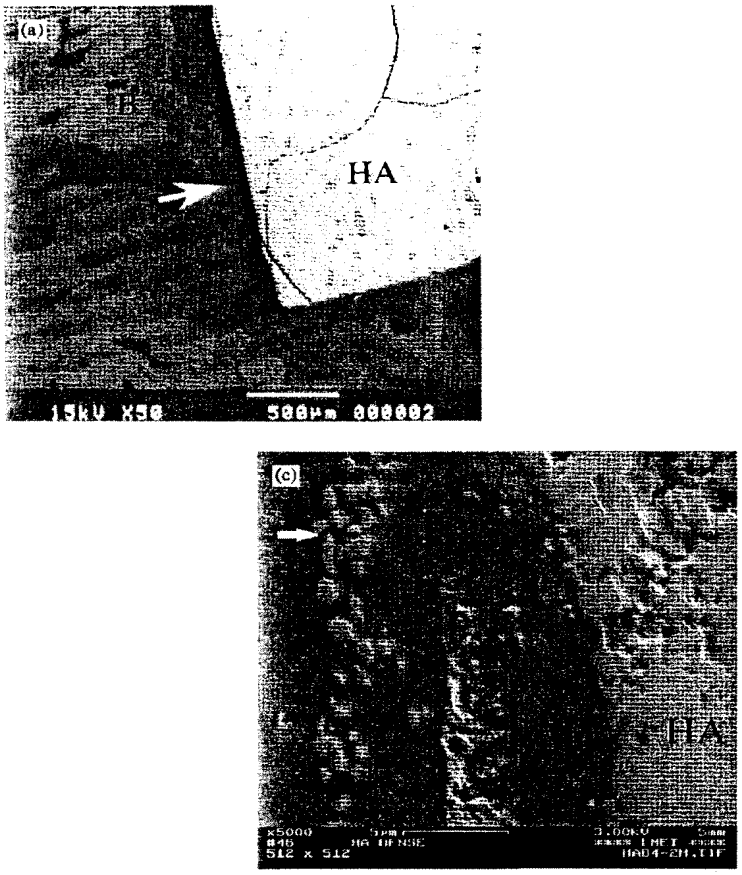

Fig. 3. (a) Back-scattered electron micrograph showing the immature bone tissue (arrow) bridged the cortical bone (B) edges to the implant surface 2 months after implantation (magnification × 50); (b) secondary electron micrograph showing the degradation of HA interface 2 months after implantation. (Ct: connective tissue, magnification × 10 000); (c) secondary electron micrograph showing HA particles (arrow) released in soft tissues surrounding the ceramic (magnification × 20 000).

4.4. After 3 months

The HA ceramic was almost totally surrounded by lamellar bone (B) (Fig. 4a). The bone surrounding the samples showed different grey levels in the implant vicinity suggesting that the mineralization was still evolving even after newly formed bone was remodelled and had the morphological appearance of mature bone. Havers's canals with an irregular inner surface were visible at the sample surface. The resorption process which had lead to the formation of these canals in the bone applied to the ceramic also. Degraded ceramic region faced the canals. However in most of the cases, most of the canal volume was located within bone suggesting that the resorption rate of bone is higher than that of the ceramic.

The implant roughness was increased after a few months (Fig. 4b). The porosity between the grains was enhanced at the material surface. A bone matrix was formed inside the pores created at the material surface even when the pores were a few µm in size (Fig. 4c). Osteocytes in close proximity to the ceramics emitted cell expansions toward the material.

4.5. Histomorphometry

The percentage of ceramic length in contact with bone increased from 2 weeks up to 3 months and was stable from 3 to 18 months (Fig. 5a). Immature bone disappeared from the interface after 9 months (Fig. 5b). The bone porosity around the implant decreased from

Fig. 4. (a) Secondary electron micrographs showing the remodelling of bone (B) occurring at HA surface 3 months after implantation (magnification × 500); (b) back-scattered electron micrograph showing the implant roughness 3 months after implantation (magnification × 1000); (c) secondary electron micrograph showing the degradation of HA interface 3 months after implantation and pores (M) interconnections (arrow) (magnification × 10 000).

2 weeks up to 3 months and at 9 months the porosity was similar to that of the cortical bone (Fig. 5c). The osteoconductive index increased until month 9. At this time, the perimeter of the implant was completely surrounded by bone (Fig. 5d).

The variation of the mean thickness of the region under the ceramic surface is not linear (Fig. 5e).

4.6. EDX Results

The X-ray profiles of calcium and phosphorus intensities at the bone-HA interface are represented in Figs. 6–8. Ca and P amounts are, respectively, higher in HA than in cortical bone (Tables 1 and 2). Their concentrations in HA and in bone stay, respectively, at the same level. The concentrations of Ca and P at the interface increase according to the time after implantation. The evolution of these two elements represent the bone ingrowth at the HA periphery. After two months of implantation the ceramic is surrounded by bone.

5. Discussion

This study shows that integration of dense ceramics occurs in several phases. There is a difference between the ossification of dense and porous ceramics. There is no osteoblast differentiation and immobilization at the dense ceramic surface. There is only a centripetal ossification, i.e., the bone coming from the edges of the implantation cavity. The persistence of immature bone at the interface with the material is slow. When resorption

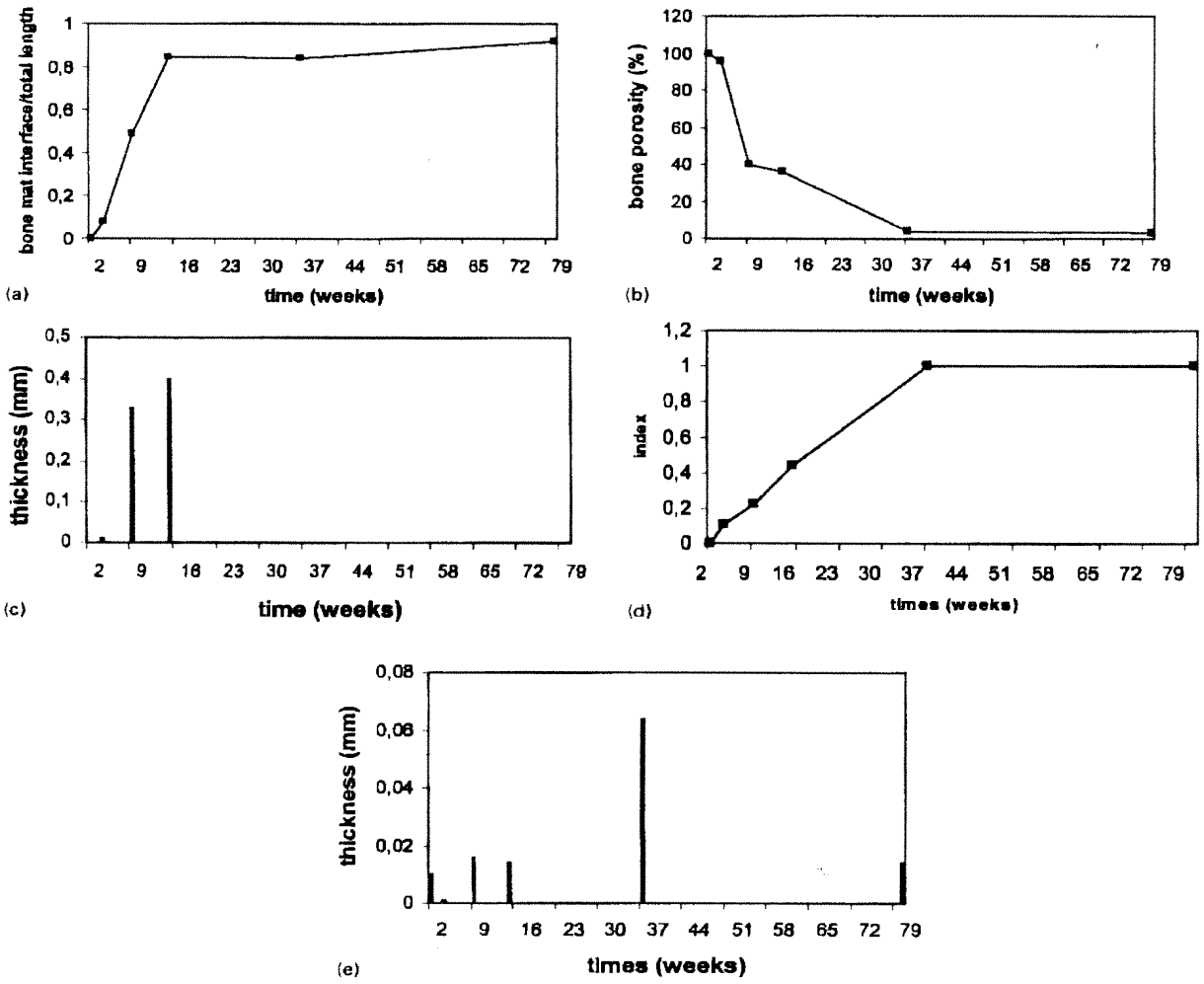

Fig. 5. (a) Ratio of the length of material in contact with bone to total length vs time of implantation (osseointegration index); (b) percentage of bone porosity in a 0.5 mm thick zone around the implant vs implantation time; (c) thickness of immature bone zone in contact with a 1 mm length of the implant perimeter; (d) osteoconductivity index: length of ceramic in the bone marrow cavity coated by bone/total length in the bone marrow cavity vs time; (e) mean thickness of 0.1 mm high zone under the surface of the ceramic vs time.

cavities of the immature bone were in contact with the ceramic surface, the resorption concerned also the ceramic although to a lesser extent. This suggests that most of the ceramic resorption will occur in the early period before the woven bone is replaced by mature bone tissue because the remodelling rate is much higher during this period.

This study has shown that dense HA-ceramic is very poorly degraded when implanted in cortical bone. A few μm thick layer is degraded within 18 months. This degradation is much lower than in the creeping substitution process usually seen at the surface of porous ceramics. No degradation could be measured before 9 months of implantation suggesting a low resorption rate during the early period. The software used could not permit the measurement of the different roughness parameters. However, the results found show that the degradation of the ceramic is not linear, some limited regions shows resorption marks while other are intact after 9 months. The implanted ceramics showed default zones marked by an increased porosity between the ceramic grains. These zones appear to be homogeneously dispersed in the ceramic matrix. When they are close to the surface, they constitute a high degradation rate region which increases

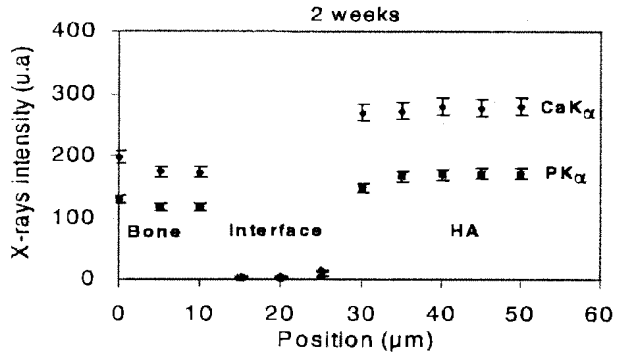

Fig. 6. X-ray intensity profiles of Ca K_α and P K_β 2 weeks after implantation.

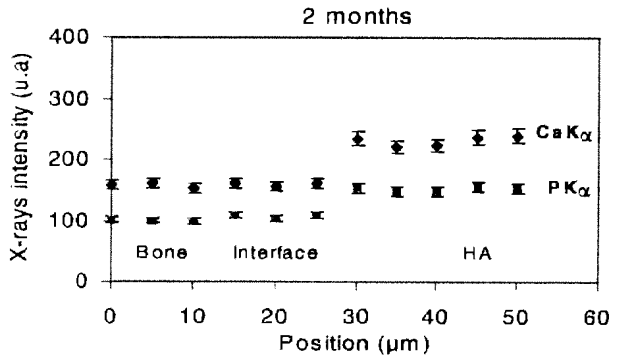

Fig. 7. X-ray intensity profiles of Ca K_α and P K_β 2 months after implantation.

the ability of bone to degrade the material. It indicates that any manufacturing process which avoids the presence of these zones will greatly reduce the degradation rate of these ceramics.

Although the samples were made of a calcium phosphate phase very close to that of bone, their degradation rate was much lower than that of the bone as was suggested by the asymmetry of the resorption cavity in contact with the material surface. It suggests that characteristics other than chemical composition have a tremendous influence on their resorption rate and their biological behaviour.

Bone is composed of a type A or AB poorly crystallized apatite whose crystals have a peculiar shape and are associated with organic macromolecules. Conversely, the ceramics are constituted by highly crystalline HA whose grains are closely packed and have a surface area lower than that of bone due to their shape and density. These differences are certainly responsible for the differences in the behaviour of both materials when implanted in

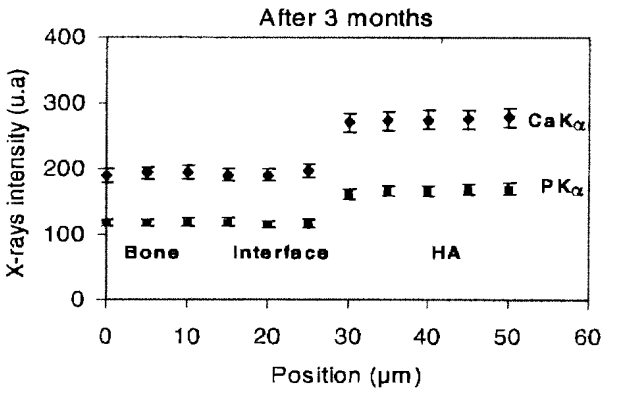

Fig. 8. X-ray intensity profiles of Ca K_α and P K_β 3 months after implantation.

Table 1
Calcium X-ray mean intensities in bone, at bone/HA interface and in HA relative to time after implantation

	X-ray mean intensity in bone	X-ray mean intensity at bone/HA Interface	X-ray mean intensity in HA
2 Weeks	182 ± 13	7 ± 6	274 ± 6
2 Months	158 ± 4		231 ± 9
After 3 months	193 ± 3	—	275 ± 3

Table 2
Phosphorus X-ray mean intensities in bone, at bone/HA interface and in HA relative to time after implantation

	X-ray mean intensity in bone	X-ray mean intensity at bone/HA Interface	X-ray mean intensity in HA
2 Weeks	122 ± 7	3 ± 2	165 ± 9
2 Months	105 ± 5	—	147 ± 13
After 3 months	117 ± 2	—	167 ± 3

osseous site. The dense HA ceramics with low surface can be considered as non degradable if we consider negligible the few μm disappearing from the ceramic surface.

The osteoconductivity of the material made bone formation possible in a region which did not contain bone previously. The osteoconductive index increased rapidly until the material was totally coated by bone even in the bone marrow cavity showing that the length of conduction can be high.

The superimposition of porosity curves on those of the integration osseointegration index shows a period ranging from 3 to 9 months, in which the implant is

totally in contact with bone and whose porosity decreased. This suggests that the remodelling process at the ceramic contact is very high during this period.

6. Conclusions

Dense HA in cortical bone is integrated by a bone apposition process with very limited degradation. This degradation is enhanced by the defaults found in the ceramic and could be reduced to almost nothing if the characteristics of the ceramic are improved. Dense HA ceramics can be of interest for high compressive strength bioactive materials.

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